10/799,406 Page 3

chain nodes : 17 18 20 21 22

ring nodes :

chain bonds : 4-22 9-10 11-20

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-15 11-12 12-13 13-14

14-15

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 4-22 5-6 5-7 6-9 7-8 8-9 9-10 10-11 10-15 11-12

11-20 12-13 13-14 14-15

isolated ring systems :

containing 1 : 10 :

G1:C,N

G2: CH3, X

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 17:CLASS 18:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR

G1 C,N

G2 Me,X

<10/07/2005>

Habte

Broad search For 10/799,404 10/799,406 10/799,407 10/799,406 Page 4

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 09:24:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 7 TO ITERATE

100.0% PROCESSED 7 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 7 TO 298
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s ll sss full

FULL SEARCH INITIATED 09:24:28 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 87 TO ITERATE

100.0% PROCESSED 87 ITERATIONS 8 ANSWERS

SEARCH TIME: 00.00.01

L3 8 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST

161.33
161.54

FILE 'CAPLUS' ENTERED AT 09:24:33 ON 07 OCT 2005
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FILE COVERS 1907 - 7 Oct 2005 VOL 143 ISS 16 FILE LAST UPDATED: 6 Oct 2005 (20051006/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13

L4 3 L3

<10/07/2005>

Habte

10/799,406 Page 5

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS OD STN ACCESSION NUMBER: 2004:857604 CAPLUS DOCUMENT NUMBER: 141:332205

DOCUMENT NUMBER:

141:332205
Preparation of pyrrolo[1,2-b]pyridazine compounds as CRF receptor antagonists for the treatment of disorders such as anxiety and depression Fu, Jian-min
Pharmacia & Upjohn Company, USA
PCT Int. Appl., 26 pp.
CODEM: PIXXD2
Patent TITLE:

INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

WO 2004087708
A1 20041014
WO 2004-1B1006
20040322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, 1D, 1L, 1N, 1S, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LW, MA, MD, MG, MK, MM, MW, MK, AZ, NA, NI, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VN, VU, ZA, ZM, ZF, RW; BW, GH, GM, KZ, MN, NI, AT, BE, BG, CH, CT, CZ, DE, DK, ES, ST, FT, FR, BF, BJ, CF, CG, CI, CH, GA, GN, GQ, GW, ML, MR, NE, SN, TU, SAD0420887
A1 20041021

NS 2004209887
A1 20041021

NS 2004209887
A1 20041021

NS 2004-799404

RITY APPLIA INFO: US 2004-799404 US 2003-460698P PRIORITY APPLN. INFO.:

ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

773086-73-0 CAPLUS
Pyrrolo[1,2-8)pyridazin-4-amine, 7-(4-methoxy-2-methylphenyl)-2,6-dimethylN-(1-methylpropyl)- (9CI) (CA INDEX NAME)

1

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

Disclosed are novel CRF receptor antagonists and their use in the treatment of a variety of disorders, including disorders manifesting hypersecretion of GRF, or associated with CRF or CRF receptors, such as anxiety, and depression. The CRF receptor antagonists of the invention have the structure of formula I (R = H or He), including starcelsomers or nixts, of stereoisomers, pharmaceutically acceptable producys, or pharmaceutically acceptable producys, or pharmaceutically acceptable alto. Compds. I were tested in several biol. assays, and had IC50 values of less than 3 nH in a CRFI receptor binding assays, for example, 4-brono-3-nathylanisole was treated with t-Buli followed by reaction with a-mathyl-y-butyrolactome to give a ring-opened hydroxy ketone, which underwent Swern oxidation to yield the corresponding formyl ketone. This dicarbonyl compound was cyclized with N-maninophthalimide to afford pyrrole II, which was deprotected with hydrazine and then converted to hydroxybicycle III via cyclocondensation with Et trans-3-ethoxycrotonate. Bromination of III with PBr3 followed by amination of the resulting bromide with (S)-sec-butylamine led to pyrrolo[1,2-b]pyridazine (S)-I (R = H). Claimed uses also include (1) use of labeled compds. I in competitive binding assays for screening of other CRF receptor ligands, and (2) use of labeled I for detecting CRF receptors in tissues.

773086-71-8P 773086-72-9P 773086-73-0P
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRC (Pharmacological activity); SFN (Synthetic preparation); TRU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of pyrrolopyridazine derivs. as CRF receptor antagonists)

773086-71-8 CAPLUS

Pyrrolo[1,2-b] pyridazin-4-amine, 7-(4-methoxy-2-methylphenyl)-2,6-dimethyl-N-((15)-1-methylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

773086-72-9 CAPLUS
Pyrrolo(1,2-b)pyridazin-4-amins, N-(1-ethylpropyl)-7-(4-methoxy-2-methylphenyl)-2,6-dimethyl- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:857173 CAPLUS
DOCUMENT NUMBER: 141:350182
TITLE: Preparation of pyrrolo[1,2-b]pyridazine compounds and their use as CRF receptor antagonists
TNVENTOR(S): FT, Jian-min USA
SOURCE: Prizer Inc, USA
U.S. Pat Appl. Publ., 12 pp.
CODEN: USUNCO
DOCUMENT TYPE: Patent

DOCUMENT TYPE: Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

| PATENT NO. KIND | | | | | | D | DATE | | | APPL | DATE | | | | | | | | |
|-----------------|------------|-----|-----|-----|----------|-------------|------|------|------------------|----------------|------|-----|-----|-----|-----|----------|----------|--|--|
| | | | | | | | | | | | | | | | | | | | |
| US : | 2004204415 | | | | | A1 20041014 | | | 1 | US 2004-799407 | | | | | | | 20040312 | | |
| WO : | 2004087709 | | | | A1 20041 | | | 1014 | 14 WO 2004-IB951 | | | | | | | 20040322 | | | |
| | ₩: | ΑE, | AG, | AL, | AM, | AT, | AU, | AZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH | | |
| | | CN, | co, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD | | |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KE, | KG, | ΚP, | KR, | KZ, | LC | | |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MV, | MX, | MZ, | NA, | NI | | |
| | | NO, | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY | | |
| | | TJ, | TM, | TN, | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW | | |
| | RW: | BW, | GH, | GM, | ΚE, | LS, | MW, | MZ, | SD, | SL, | SZ, | TZ, | υG, | ZM, | ZW, | AM, | AZ | | |
| | | BY, | KG, | ΚZ, | MD, | RU, | TJ, | TM, | AT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE | | |
| | | ES, | FI, | FR, | GB, | GR, | HU, | IE, | IT, | LU, | MC, | NL, | PL, | PT, | RO, | SE, | SI | | |
| | | SK, | TR, | BF, | BJ, | CF, | CG, | CI, | CM, | GA, | GN, | GQ, | GW, | ML, | MR, | NE, | SN | | |
| | | TD. | | | | | | | | | | | | | | | | | |

PRIORITY APPLN. 1 OTHER SOURCE(S): NFO.: MARPAT 141:350182

The title compds. [I] R = H, Me], useful in the treatment of a variety of disorders, including disorders manifesting hypersecretion of CRF or associated with CRF or CRF receptors, such as anxiety, and depression, were prepared E.g., a multi-step synthesis of I [R = He], starting from 4-bromo-3-chloroanisole and α -methyl- γ -buttyrolactone, was given. The compds. I showed Ki of <2.0 mH in in vitro CRF1 receptor

10/799,406

Page 7

ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN (Continued) binding assay. The pharmaceutical compn. comprising the compd. I is claimed. 778345-59-09 775345-60-39 RL: PAC (Pharmacological activity), SFN (Synthetic preparation), THU (Therapeutic use); BIOL (Biological study), PREP (Preparation), USES (Uses) (preparation of pyrrolo[1,2-b]pyridazine compds. and their use as CRF receptor antagonists) 775345-59-0 CAPLUS Pyrrolo[1,2-b]pyridazin-4-amine, 7-(2-chloro-4-methoxyphenyl)-N-(1-ethylpropyl)-2,6-dimethyl- (SCI) (CA INDEX NAME)

775345-60-3 CAPLUS
Pyrrolo[1,2-b]pyridazin-4-amine, 7-(2-chloro-4-methoxyphenyl)-2,6-dimethyl-N-[(1S)]-1-methylpropyl]- (SCI) (CA INDEX NAME)

ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN (Continued) hypersecretion of CRF or assocd. with CRF or CRF receptors, e.g. anxiety and depression. CRF receptor antagonists of the invention have structure I (R=H, Me), including stereoisomers or mixts. of stereoisomers, pharmaceutically acceptable prodrugs, or pharmaceutically acceptable salts thereof.

pharmaceutically acceptable prodrugs, or pharmaceutically acceptable salt thereof.
773059-40-8 773059-41-9 773059-42-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pyrrolopyridazine compound CRF receptor antagonists, and use in treatment of CRF and CRF receptor-associated disorders)
773059-40-8 CAPLUS
Pyrrolof(,2-b)[pyridazin-4-amine, 7-(6-methoxy-2-methyl-3-pyridinyl)-2,6-dimethyl-N-(1-methylpropyl)- (9CI) (CA INDEX NAME)

773059-41-9 CAPLUS
Pyrrolo[1,2-b]pyridazin-4-amine, N-{1-ethylpropyl}-7-(6-methoxy-2-methyl-3-pyridinyl)-2,6-dimethyl- (9CI) (CA INDEX NAME)

773059-42-0 CAPLUS
Pyrrolo[1,2-b]pyridazin-4-amine, 7-(6-methoxy-2-methyl-3-pyridinyl)-2,6-dimethyl-M-[(iS)-1-methylpropyl)- (9C1) (CA INDEX NAME)

Absolute stereochemistry.

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L4 ANSWER 3 OF 3
ACCESSION NUMBER:
DOCUMENT NUMBER:
111TLE:
114:325761
114:325761
117TLE:
11VENTOR(S):
PATENT ASSIGNEE(S):
PATENT ASSIGNEE(S):
DOCUMENT TYPE:
LANGUAGE:
PAILUR ACC. NUM. COUNT:
PATENT TOROBRATION:
PATENT TOROBRA

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

| PAT | ENT | KIND DATE | | | APPLICATION NO. | | | | | | DATE | | | | | | |
|-------|--------------------|-----------|-----|-----|-----------------|-------------|-----|---------------|-----------------|-----|------|-----|-----|----------|------------|-----|-----|
| | | | | | | - | | | | | | | | | - | | |
| US | US 2004204414 | | | | | A1 20041014 | | | US 2004-7994D6 | | | | | | 20040312 | | |
| WO | WO 2004087710 | | | | A1 20041014 | | | WO 2004-IB971 | | | | | | 20040322 | | | |
| | W: | ΑĖ, | AG, | AL, | AM, | AΤ, | ΑU, | ΑZ, | BA, | BB, | BG, | BR, | B₩, | BY, | BZ, | CA, | CH |
| | | CN, | co, | CR. | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD |
| | | GE, | GH, | GH, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KE, | KG, | KP. | KR. | KZ, | LC |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW. | MX, | MZ, | NA, | NI |
| | | NO, | NZ, | OM, | PG, | PH, | PL, | PT. | RO, | RU, | SC, | SD, | SE, | SG, | SK. | SL, | SY |
| | | TJ, | TM, | TN, | TR. | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN. | YU, | ZA, | ZM. | ZW |
| | RW: | BW, | GH, | GM. | KE, | LS, | MV, | MZ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZV. | AM. | AZ |
| | | BY, | KG, | KZ. | MD. | RU, | TJ, | TM, | AT. | BE, | BG, | CH, | CY, | CZ, | DE, | DK. | EB |
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| | | SK, | TR. | BF. | BJ, | CF. | CG, | CI, | Œί, | GA, | GN, | GQ, | G₩, | ML, | MR. | NE. | SN. |
| | | TD, | TG | | | | | | | | | | | | | | |
| IORIT | RITY APPLN. INFO.: | | | | | | | | US 2003-459744P | | | | | | P 20030402 | | |
| | | | | | | | | | | | | | | | | | |

The invention discloses CRF receptor antagonists and their use as treatment of a variety of disorders, including disorders manifesting

ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)